

TABLE 5.—Comparison of smoking habit data obtained during life and after death

Smoking habit data obtained during life, 1971	Number	Smoking habit data obtained at death			
		Never smoked	Formerly smoked	Smoked	Smoked at some time
Never smoker	12	8	2	2	0
Ex smoker	26	2	15	2	7
Smoker	76	1	12	33	30

SOURCE: Berry et al. (1985).

and for those who have died (which would include most individuals with lung cancer) by questioning next of kin or checking hospital records. Berry and colleagues (1985) examined the comparability of these data sources in a prospective evaluation of asbestos workers in which smoking data were accumulated both at the start of the study period (i.e., prospectively) and at the time of death from lung cancer (i.e., retrospectively). A comparison of the smoking status obtained by the two methods for the same individuals is shown in Table 5. In general, there was good agreement between the two methods, but both methods identified as never smokers individuals who were classified as smokers by the other method. No data were presented to allow determination of which method was more accurate.

The random misclassification of smoking status, of itself, should not introduce spurious associations for the population as a whole, or for the smokers in the population (Greenland 1980). However, when the question being asked is whether a risk exists in the absence of smoking and synergism between smoking and the occupational exposure is present, the misclassification of even small numbers of exposed smokers as nonsmokers can lead to the conclusion of increased risk of lung cancer due to an occupational exposure in the absence of cigarette smoking. The potential for misclassification exists and is of greatest concern when decisions are being made on small numbers of cases.

The second caveat that may need to be applied in the examination of the effects of occupational exposure among people who have never smoked is the potential effect of involuntary exposure to cigarette smoke. A number of studies have shown increased lung cancer risks in the nonsmoking wives of smokers, raising the question of a carcinogenic risk due to environmental tobacco smoke exposure (IARC, in press). If these studies can be extrapolated to the workplace, then the potential exists for environmental tobacco smoke in the worksite to act as an occupational carcinogen,

particularly in those occupations in which there is a high prevalence of active smoking among workers.

The considerations raised by examination of smokers with workplace exposures are somewhat different from those raised by examination of nonsmokers. Comparisons of smokers with and without an occupational exposure require careful attention to the correlations among age, duration of exposure, and smoking dose. Age adjustment of the death rates in the exposed group and the control population is generally accepted as more useful than simply comparing the mean age of the two populations, because of the rapid rise in lung cancer death rates in the older age groups. It is less widely understood that age adjustment does not eliminate the effects of differences in the age distributions of smokers between the two populations. The smoking-related risk of developing lung cancer occurs disproportionately in older smokers compared with younger smokers. Therefore, in two populations with similar prevalences of smoking, but with different age distributions of that smoking prevalence, the population with the higher prevalence of smoking in the older age group will have the higher number of lung cancer deaths. This difference in number of lung cancers will persist after an age adjustment using the age distributions of the entire population (smoker and nonsmoker). Therefore, in considering the differences between occupationally exposed smokers and smokers who are not exposed, the lung cancer deaths should be adjusted for age on the basis of the age distribution of the smokers in the two populations rather than the age distribution of the entire population.

Several attempts have been made to combine the strengths of large population-based measurements with the detailed measurements of smoking status available in cohort studies. Hammond and colleagues (1979) used the American Cancer Society (ACS) study of 1 million men and women to develop a control group for a study of asbestos insulation workers. From the ACS study population, they extracted a group of more than 73,000 men who were white, not a farmer, had no more than high school education; did have a history of occupational exposure to dust, fumes, vapors, gases, chemicals, or radiation; and were alive at the time of the initiation of followup of the insulators. From this control group, they were able to develop age-specific and smoking-specific expected lung cancer death rates for comparison with the observed death rates in the insulation workers. There was a difference in the time period of followup between these two studies; therefore, the expected lung cancer death rates were adjusted upward on the basis of differences in the national lung cancer death rates during the years of differential followup. This approach allowed the expected rates to be calculated from a large enough population to provide stable rates in a number of separate age and smoking categories. The control group and the

exposed populations were also matched for a number of those characteristics that raise questions about the comparability of national death rate data to populations of employed workers.

A somewhat different approach to the same problem was taken by Berry and colleagues (1985). They used data from a prospective mortality study of British physicians by smoking status (Doll and Peto 1978, 1981) to develop factors that related the risks of smokers, nonsmokers, and ex-smokers separately to the risk in the entire population of physicians. They calculated the expected number of deaths for the exposed workers in each smoking category, using national death rate data, and multiplied this expected number of deaths by the smoking factor to get a smoking-specific expected number of deaths for each category of exposed workers. They also adjusted the number of expected deaths for differences in geographic location by multiplying the expected deaths by the ratio of the local lung cancer SMR to the national lung cancer SMR. This approach is obviously quite sensitive to the method by which the smoking-specific factors are developed, and it is not clear that one set of factors can be applied to all ages.

When an explicit control population is being used, the differences in smoking behavior can be controlled through the use of a statistical model for lung cancer risk in the population. Models may include a variety of measures of cigarette smoking dosage and duration, and the mortality experienced by the exposed population can be examined by using the risk model developed in the control population. This approach allows the confounding due to smoking to be adjusted through the use of terms for intensity and duration of exposure.

Comparisons Using Internal Control Populations

The use of an internal control group drawn from the same workforce as the exposed population, but not exposed to the agent of interest, may produce a control group that is more closely matched to the exposed population than the total U.S. population would be (Breslow et al. 1983; Pasternack and Shore 1976; Redmond and Breslin 1975). Working populations tend to have a lower overall mortality than the U.S. population of the same ages (McMichael 1976; Enterline 1975; Fox and Collier 1976; Shindell et al. 1978; Vinni and Hakama 1980), at least in part because workers with illness tend to drop out of the working population. This lower mortality has been called the healthy worker effect and is one of the reasons the selection of an internal control population may be more appropriate than using SMRs for evaluating occupational exposure risks. External control groups, selected from populations geographically or demographically similar to the exposed population, may also provide a population more similar to the exposed workers than the general U.S. population.

That the smoking behaviors of the exposed group and the control population are comparable must still be established. The selection of a control population based on its similarity in one variable (such as worksite) does not allow the assumption of comparability on other variables (such as smoking behaviors). It is possible for a control population to deviate from national measures of smoking behavior in one direction and for the exposed population to deviate in the opposite direction; thus it is important to actually examine the comparability of the smoking behaviors in the exposed group and the control population even when an internal control population is used.

The absence of an external control group means that the entire population has some exposure. Potential confounding of cumulative occupational exposure by cumulative smoking exposure can be reduced by stratification of the two exposures in question. The risk with increasing exposure to an occupational agent can then be examined within each strata of smoking exposure. Stratification of smoking by intensity only (cigarettes per day) would lead to a residual confounding of smoking and cumulative dust exposure, owing to the importance of duration of smoking for lung cancer risk and the association of age with both duration of smoking and cumulative dust exposure.

The reduction of residual confounding should also guide the selection of the number of strata selected for smoking and the occupational exposure. The larger the risk due to smoking in relation to the risk due to the occupational exposure, the larger the number of smoking strata needed to control the confounding. The use of too few strata may result in the residual confounding producing the appearance of a dose-response relationship with the occupational exposure.

A second method of controlling the confounding of occupational exposure by smoking behaviors is through the use of modeling techniques. By using a multiple logistic regression, a model of the smoking variables that contribute to lung cancer risk can be developed. The model should include measures of intensity and duration as well as a factor for cessation. Other factors that may contribute to the model are type of cigarette smoked, use of pipes or cigars, and age of initiation (as separate from duration). Once the model is established for smoking variables, a term or terms for the occupational exposure can be added to the risk prediction equation and tested to see whether the term improves the fit of the model to the observed data.

Case-control analyses can also be applied in the absence of an external control group by examining the distribution of exposures in cases of lung cancer and in a control group selected from the sample population of workers, but who have not died of lung cancer. Confounding due to cigarette smoking can then be controlled by

stratification (Liddell et al. 1984) or by modeling (Whittemore and McMillan 1983; Pathak et al., in press). This approach is particularly useful when a case-control analysis can be nested within an ongoing study of a cohort of workers. In this setting, the smoking habits of the workforce are often known prior to the development of lung cancer, eliminating the potential for biased recall of smoking habits by the lung cancer patients (or their survivors) compared with the controls.

Examination of Occupational Exposures When Smoking Habits Are Not Known

In many occupational settings the smoking habits of the workforce are either unavailable or incompletely ascertained. In these cases, the death rates for these workers are compared with rates for a control population or with national mortality data (to generate an SMR). The potential for smoking pattern differences to influence the SMR is then evaluated by calculating the maximal distortion that would be produced, assuming that the exposed population had a very high smoking prevalence. The calculations used are similar to those used in generating Tables 2 and 3. As discussed earlier, extremes of differences in smoking prevalence and dosage could be expected to generate SMRs in excess of 200, and differences in age distribution and type of cigarette smoked may increase this number even more. Once an outer limit for smoking-related distortions of the SMR is estimated, it becomes the value that must be below (outside) the confidence interval surrounding the actual SMR for the exposed population in order to exclude a potential smoking effect. This approach may be useful in settings where smoking data are unobtainable, but should not be used as a substitute for collecting smoking information.

When the mortality in a control population is compared with the mortality of an exposed population in the absence of smoking data, the potential for differences between the smoking habits of the two populations may be larger than the differences when using SMRs. The control group and the exposed population may deviate in opposite directions from the mean smoking behaviors represented in the SMR, and correspondingly, the differences in cancer outcome may also be magnified.

One method of adjusting for differences in smoking patterns between populations when smoking data are not available, or would be too costly to obtain, is to survey a random sample of the two populations for smoking behavior. The limitation of this technique is that the sample size needed to obtain estimates of usable precision is large and may approximate the size of the two populations combined.

An additional method of examining the effects of unknown differences in smoking habits on the rates of one smoking-related cancer is to look at the rates of other smoking-related cancers in the same population. The various smoking-associated cancers do not all have the same incidence rates, rate of change in incidence with time, ethnic distribution, cure rate, or age distribution. These differences make cross-comparison between rates of these cancers as a measure of differences in smoking patterns between populations a complex and uncertain exercise at best. This kind of comparison may be useful as a point of discussion, but probably offers little in the way of an estimate of the differences between populations in their smoking behavior.

Summary and Conclusions

1. Cigarette smoking and occupational exposures may interact biologically, within a given statistical model and in their public health consequences. The demonstration of an interaction at one of these levels does not always characterize the nature of the interaction at the other levels.
2. Information on smoking behaviors should be collected as part of the health screening of all workers and made a part of their permanent exposure record.
3. Examination of the smoking behavior of an exposed population should include measures of smoking prevalence, smoking dose, and duration of smoking.
4. Differences in age of onset of exposure to cigarette smoke and occupational exposures should be considered when evaluating studies of occupational exposure, particularly when the exposed population is relatively young or the exposure is of relatively recent onset.

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CHAPTER 4

EVALUATION OF CHRONIC LUNG DISEASE IN THE WORKPLACE

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Introduction

Exposure to harmful agents in the workplace is, and will probably continue to be, an important and avoidable cause of both acute and chronic lung diseases. The major chronic lung diseases associated with workplace exposures can be classified as the pneumoconioses (fibrotic diseases of the lung parenchyma secondary to dust inhalation), industrial bronchitis and other processes involving the lung's airways, and occupational asthma. Some of these diseases were recognized long before cigarette smoking became prevalent. During the 16th century, Agricola and Paracelsus described diseases of miners (Hunter 1978); early in the 18th century, Ramazzini (1940) reported further on the respiratory problems of miners and noted that the lungs of stonecutters were full of sand. Occupational lung disease in coal miners was recognized during the 1800s (Morgan 1984a).

In the 20th century, many chronic lung diseases caused by workplace exposures have been studied intensively using epidemiological, physiological, and clinical approaches. The resulting data have been essential for developing the standards that govern workplace exposures and for evaluating worker safety. In this century, however, assessment of the effects of occupational agents on the lung has been made difficult by the widespread smoking of cigarettes. This behavior has been particularly prevalent among those at high risk for occupational lung diseases—men employed in blue-collar jobs (US DHEW 1979b).

The degree of pulmonary impairment in any individual represents the summation of the effects of all harmful environmental factors, including cigarette smoking, occupational agents, and other exposures. Cigarette smoking, in the absence of other exposures, causes chronic bronchitis (cough and mucous hypersecretion), airway abnormalities, and emphysema (abnormal dilation of the distal airspaces with destruction of alveolar walls); together, the last two disease processes underlie the expiratory flow limitation found in chronic obstructive lung disease (COLD) (US DHHS 1984). Cigarette smoking may potentiate the effects of some occupational agents on the lung. This potentiation may occur through an effect of cigarette smoke on the mechanism of lung injury that results from a given occupational exposure, or it may result from a mechanism of lung injury due to cigarette smoke that is independent of the mechanism of occupational injury but produces a level of combined lung damage capable of potentiating the level of disability or the level of abnormality detected by pulmonary function tests, x rays, or symptoms. The term "synergism" is used in this chapter to refer to an effect of combined exposure to cigarette smoke and occupational agents that results in a level of abnormality (by whatever measure being used) that is significantly greater than the sum of the levels of abnormality

produced by the agents separately. Such interactions are of importance not only for researchers but also for the exposed workers and their employers. Synergism between cigarette smoking and occupational agents may, at the individual level, markedly raise the risk of developing disease and, at the group level, greatly increase the burden of occupational disease in the workforce. Thus, in evaluating the effects of workplace exposures on the lung, consideration must be given not only to the independent effects of cigarette smoking and of the agent of interest but also to the possible interaction of these factors.

This chapter describes the techniques used to evaluate chronic lung disease in the workplace and addresses the methodological issues raised by cigarette smoking. The focus of the chapter is largely confined to the chronic, fixed lung injuries that result from these exposures rather than the acute reversible responses that characterize occupational asthma. This focus was adopted in the interest of clarity and brevity and does not suggest that the issues related to the evaluation of occupational asthma are either unimportant or unrelated to cigarette smoking. Emphasis is placed on methodological problems; specific exposures are reviewed in other chapters of this Report.

Chronic Lung Diseases

Sources of Information

Although cigarette smoking is the predominant cause of preventable morbidity and mortality from respiratory diseases in the United States (US DHHS 1984), occupational exposures also produce substantial disease. Because the occurrence of nonmalignant respiratory diseases is not directly monitored, its frequency must be estimated from diverse information sources such as the National Center for Health Statistics, the U.S. Bureau of Labor Statistics, the Social Security Administration, and epidemiologic surveys. The extent to which chronic lung diseases are ascertained by these sources is difficult to establish, but coverage is probably not comprehensive.

Vital statistics enumerate the numbers of deaths from specific causes. Chronic conditions, such as respiratory diseases, may be listed on the death certificate, but remain uncoded unless they led directly to death. For example, Rank and Bal (1984) reviewed death certificates and found that in comparison with its frequency as an underlying cause of death, emphysema was listed nearly twice as often as an uncoded "other" condition. Vital statistics data cannot readily be used for addressing questions related to the pulmonary effects of cigarette smoking and occupational exposures. Cigarette smoking is not included on the death certificate, and only usual

TABLE 1.—Number of deaths in selected categories of the International Classification of Diseases (ICD), for three time periods, United States

Cause of death	Year (classification)		
	1960 (ICD)	1970 (ICD)	1980 (ICD)
COLD			
Chronic bronchitis	2,287 (502)	5,014 (491)	3,269 (491)
Emphysema	9,253 (527.1)	22,721 (492)	13,877 (492)
Chronic airways obstruction n.e.c. ¹	—	4,444 (519.3)	34,743 (496)
Occupational disorders			
Coal workers' pneumoconiosis	810 (523.1)	1,160 (515.1)	982 (500)
Asbestosis	21 (523.2)	26 (515.2)	101 (501)
Silicosis	550 (523.0)	355 (515.0)	207 (502)
Other inorganic dusts	—	13 (516.0)	8 (503)
Other dusts	62 (524)	7 (516.1)	3 (504)
Unspecified	210 (523.3)		281 (505)
Conditions due to chemical fumes/vapors	—	5 (516.2)	43 (506)
Chronic interstitial pneumonia	3,973 (525)	3,351 (517)	202 (516.3)

¹ Not elsewhere classified.

SOURCE: US DHEW (1963); National Center for Health Statistics (1974), unpublished data (1980).

occupation and industry are noted. Further, the occupational information is not routinely coded by States (Kaminski et al. 1981).

Cause of death is coded according to the International Classification of Diseases, currently in its ninth revision (WHO 1977). For the chronic respiratory diseases, separate categories cover the obstructive disorders, major pneumoconioses, and other interstitial diseases (Table 1). As the International Classification of Diseases has been modified from the seventh through the ninth revisions, major changes in the coding of chronic respiratory diseases have been made. The categories for occupational lung diseases have been expanded and their titles have been made more specific. With the eighth revision (US DHEW 1968), a category (519.3) was added for the diagnosis of chronic obstructive lung disease (COLD). These changes must be considered in examining time trends of mortality. For example, after the introduction of a category for COLD, the number of deaths assigned to this code increased and deaths attributed to emphysema decreased (Table 1).

Estimates of disease occurrence based on vital statistics must be interpreted with caution. Some causes of death may be underreported, and mortality rates may not directly reflect incidence. The mortality rate for a particular disease approximates the incidence rate as the case-fatality rate approaches unity (Kleinbaum et al. 1982). Competing causes of death will also influence the relationship between incidence and mortality (Kleinbaum et al. 1982). For example, Berry (1981a) examined the mortality of 665 men certified as having asbestosis by medical boards in England and Wales. Of the 283 deaths, 39 percent were from lung cancer, 9 percent were from mesothelioma, and only 20 percent were from asbestosis. The distribution of competing causes of death should be different in smokers and nonsmokers; thus, even for non-smoking-related occupational lung diseases the relationship between incidence and mortality may vary with smoking practices.

For several respiratory diseases, vital statistics underestimate mortality. For COLD, Mitchell and colleagues (1971) compared cause of death, as reported on the death certificate, with clinical and autopsy-derived diagnoses. In 211 subjects who died of COLD, as determined by autopsy, another cause of death was listed on the death certificate for 51. For asbestosis, Hammond and colleagues (1979) used "the best available medical information" and identified 160 deaths from this pneumoconiosis in a cohort study of asbestos workers. Only 76 were similarly classified by the death certificate statement of cause of death.

State workmen's compensation claims are another source of information about the occurrence of occupational lung diseases. However, most workmen's compensation claims involve acute problems (Whorton 1983) and may more accurately measure conditions associated with irritant gas or vapor inhalation than with the pneumoconioses.

Under the Occupational Safety and Health Act, selected employers are required to maintain records of occupational injury and illness (US House of Representatives 1984). In an annual survey, the Bureau of Labor Statistics collects and reports the injury and illness data. During 1982, 2,000 reports for dust diseases of the lungs and 8,800 for respiratory conditions due to toxic agents were filed, but more specific diagnoses were unavailable (US DOL 1984). In the introduction to the 1982 survey, it was acknowledged that "to the extent that occupational illnesses are unrecognized and therefore unreported, the survey estimates understate their occurrence" (US DOL 1984, p. 3).

On a national level, the Social Security Administration operates a compensation program for people who have been disabled for at least 5 months (US DHHS 1983). People receiving compensation for chronic lung diseases must meet this criterion as well as stringent

requirements for the extent of impairment on lung function testing (US DHEW 1979a). Data from the Social Security Administration probably underestimate the prevalence of most chronic lung diseases. For example, Epler and colleagues (1980) showed that approximately 9 percent of a series of clinically diagnosed patients with pneumoconiosis met the Social Security disability criteria.

Epidemiological surveys offer the most accurate estimates of disease frequency, though the surveyed populations are generally limited to employed workers and disease frequency may therefore be underestimated. Estimates of disease frequency from a particular survey should be generalized cautiously. Nonrandom selection of occupational groups for study as well as the nonrandom enrollment of workers within a particular workforce may introduce bias.

Occurrence of Chronic Lung Diseases

Although the available data sources have limitations, they can be used to document the relative frequencies of cigarette-related and occupation-related chronic lung diseases. Most indicate that the diseases associated with cigarette smoking are much more common in the general population than those resulting from occupational exposures.

In recent years, mortality from COLD has steadily increased; the number of deaths rose from 32,179 in 1970 to 51,889 in 1980 (Table 1). The 1984 Surgeon General's Report, *The Health Consequences of Smoking: Chronic Obstructive Lung Disease* (US DHHS 1984), offered the estimate that 60,000 people would die from COLD during that year. Examination of COLD mortality rates for smokers and nonsmokers suggests that 85 to 90 percent of COLD deaths in the United States can be attributed to cigarette smoking (US DHHS 1984).

As described in the 1984 Surgeon General's Report, numerous surveys provide estimates of the prevalence of COLD (US DHHS 1984). Representative recent data have been collected in Tucson, Arizona, in six other U.S. cities, and nationwide in the National Health Interview Survey (NHIS). Lebowitz and colleagues (1975) sampled 3,805 subjects in Tucson from 1972 through 1974. In men over 44 years of age, physician-diagnosed chronic bronchitis and emphysema were reported to be 10.2 and 13.3 percent, respectively. In women over 44 years of age, the percentage with chronic bronchitis was 9.0 percent and with emphysema, 4.3 percent. From 1974 through 1977, Ferris and colleagues (1978) surveyed 7,909 men and women in six U.S. cities; 5 percent of the men and 1.9 percent of the women had airway obstruction, defined as a ratio of forced expiratory volume in 1 second (FEV_1) to forced vital capacity (FVC) less than or equal to 60 percent. The 1970 NHIS included about 116,000 persons in a nationwide sample (NCHS 1974). Individuals 19

years of age and older were asked whether they or other family members not present at the time of the interview had bronchitis or emphysema during the previous 12 months. On the basis of this survey, 3.4 million Americans over 45 years of age were projected as having chronic bronchitis or emphysema. In contrast, data from the Social Security Administration, not included in the 1984 Surgeon General's Report, showed only 20,246 new claimants for COLD receiving disability benefits in 1979 (US DHHS 1983).

The available data sources also probably do not comprehensively document the nationwide occurrence of occupational lung diseases. The number of deaths recorded as due to several occupational lung diseases was stable from 1960 to 1980 (Table 1), but it is unlikely that these death certificate data provide accurate estimates of the actual prevalence or severity of these disease processes in the U.S. population, owing to the inaccurate reporting of these diseases as cause of death. The Social Security Administration is also an ongoing source of information. In 1977, 820 persons were granted disability for pneumoconiosis; in 1979, the number had decreased to 389 (US DHHS 1983). Data from the 1970 NHIS provide an estimate of the prevalence of work-related chronic lung diseases across the Nation (NCHS 1974). Participants were queried concerning dust in the lungs, silicosis, or pneumoconiosis during the previous 12 months; their responses were used to estimate that 126,000 people nationwide had these conditions.

Numerous workforces in the United States and elsewhere have been surveyed to establish the prevalence of occupational and nonoccupational lung diseases. Representative recent surveys of workers in the United States are presented in Table 2, showing the prevalence of disease and of cigarette smoking. Various disease indicators were considered in these studies. Chronic bronchitis was diagnosed on the basis of persistent cough and phlegm as ascertained by questionnaire. For the pneumoconioses, the presence of disease was based on the presence of radiographic abnormality. Of note is the high prevalence of coal workers' pneumoconiosis reported by Morgan and colleagues (1973). A different group of readers subsequently reinterpreted the chest films reported in the Morgan and colleagues study and found a prevalence of only 12 percent; this lower prevalence suggests overinterpretation on the initial reading (Morrison and Attfield 1984).

Regardless of the occupational group, cigarette smoking is common, even in workforces exposed to acknowledged respiratory hazards (Table 2). At the time the selected surveys of these workers were conducted, 1966 to 1977 for the asbestos workers (Weiss and Theodos 1978; Samet et al. 1979) and 1981 for the uranium miners (Samet et al. 1984), knowledge of the hazards of these occupations was widely disseminated and information concerning interaction

TABLE 2.—Prevalence of cigarette smoking and occupational lung disease in selected survey populations

Study, location, years of study	Study population	Prevalence of smoking (per 100)		Prevalence of disease* (per 100)	
Kibelstis et al. (1973), U.S., 1969	8,555 coal miners	Smokers	51	Chronic bronchitis	
		Ex-smokers	24	Smokers	38
		Nonsmokers	25	Ex-smokers	30
				Nonsmokers	25
				Airway obstruction ¹	
				Smokers	18
				Ex-smokers	14
				Nonsmokers	6
Morgan et al. (1973), U.S., 1969	9,076 coal miners			Coal workers' pneumoconiosis	
				Simple	30.0
				Complicated	2.5
Weiss and Theodos (1978), U.S., 1975	88 workers from two asbestos manufacturing plants	Smokers	56	X-ray profusion	
		Ex-smokers	23	≥ 1/0	20
		Nonsmokers	21		
Samet et al. (1979), U.S., 1966-1977	409 workers from two asbestos manufacturing plants and two shipyards	Smokers	40-60	X-ray profusion	
		Ex-smokers	27-42	≥ 1/0	12-31
		Nonsmokers	10-18	≥ 2/1	5-13
Theriault et al. (1974), U.S., 1971	792 granite shed workers	Exposed workers		X-ray profusion	
		Smokers	61	1/0	21
		Ex-smokers	25	2/0	7
		Nonsmokers	13	3/0	2
Samet et al. (1984), U.S., 1981	192 uranium miners	Smokers	43	X-ray profusion	
		Ex-smokers	39	≥ 1/0	8.0
		Nonsmokers	19		
				Chronic cough/phlegm	
				< 10 years mining	52
				10-19 years mining	46
				≥ 20 years mining	59
Merchant et al. (1973), U.S., 1970-1971	787 male, 473 female cotton textile mill workers	M	W	Byssinosis	
		Smokers	63	M	W
		Ex-smokers	16	Current smokers	25
		Nonsmokers	21	Never smokers	18
			50		15
Do Pico et al. (1977), U.S., 1974	300 grain workers	Smokers	59	Chronic bronchitis	
		Ex-smokers	22	Smokers	42
		Nonsmokers	19	Nonsmokers	30
Gruchow et al. (1981), U.S.	1,510 farm workers	Smokers	15	Farmers lung disease	
		Ex-smokers	27		0.5
		Nonsmokers	57		

*Significant airway obstruction defined as an FEV₁/FVC ratio less than two standard deviations below predicted mean.

with cigarette smoking was accumulating. Nevertheless, a large proportion of the participants in these surveys smoked cigarettes. The findings from these surveys with regard to the prevalence of smoking are supported by larger data sets collected from population samples (Friedman et al. 1973; Sterling and Weinkam 1976). Friedman and colleagues (1973) questioned 70,289 participants in the Kaiser-Permanente Multiphasic Health Checkups program and found a higher proportion of smokers in those reporting occupational exposure to asbestos, silica, or fumes. Similarly, Sterling and Weinkam (1976) examined smoking patterns by employment status in data from the 1970 NHIS and found the prevalence of smoking to be highest among blue-collar workers. Association between occupational group and cigarette smoking practices is addressed in detail elsewhere in this Report.

Thus, in research and clinical care related to chronic occupational lung diseases, consideration must be given not only to occupational exposures but also to cigarette smoking. The remainder of this chapter describes the general patterns of lung injury by cigarette smoking and occupational exposures and the methods used for evaluating workers who are exposed to both.

Patterns of Lung Injury

The sites of lung injury caused by cigarette smoke and occupational agents may be broadly categorized as the large airways, the small airways, and the parenchyma. The effects of cigarette smoke on these sites are summarized in Table 3. A comparison of injury patterns from cigarette smoke and from selected, but representative, occupational exposures follows.

Injury From Cigarette Smoke

The pattern of lung injury associated with cigarette smoking has been comprehensively described elsewhere (US DHHS 1984). In the large airways, cigarette smoke causes an increase in mucous gland size and in goblet cell number. These changes result in increased mucus production and the associated symptom of chronic bronchitis. Large airway injury may contribute to airflow obstruction, but the peripheral airways are the predominant site of the increased airflow resistance in COLD (US DHHS 1984).

Changes in the small airways are one of the earliest manifestations of cigarette smoking. Niewoehner and colleagues (1974) examined the lungs of 20 smokers and 19 nonsmokers who died suddenly at a mean age of 25 years. A pattern of small airways injury, termed "respiratory bronchiolitis," was readily identified, even in these young smokers. Clusters of brown pigmented macrophages were found in the respiratory bronchioles, which also displayed increased

TABLE 3.—Pathologic changes and manifestations of lung injury by cigarette smoke

	Large airways	Small airways	Parenchyma
Pathologic changes	Mucous gland hyperplasia, inflammation and edema, ↑ bronchial smooth muscle	Goblet cell metaplasia, inflammation and fibrosis of the respiratory bronchiole	Emphysema, minimal interstitial fibrosis
Manifestations			
Symptoms	Cough, phlegm	Cough, phlegm	Dyspnea
Physical signs	None	Crackles	Diminished breath sounds
X ray	None	? Linear opacities	? Linear opacities
Pulmonary function testing	? ↓ FEV ₁	↓ FEV ₁ , ↓ FEV ₁ %, • TLC, ↑ RV, ↓ DLCO	↓ FEV ₁ , ↓ FEV ₁ %, • TLC, ↑ RV, ↓ DLCO
		Accelerated annual decline of FEV ₁	Accelerated annual decline of FEV ₁

numbers of inflammatory cells and denuded epithelium. To characterize the physiological consequences of small airways injury associated with smoking cigarettes, Cosio and colleagues (1978) correlated small airways morphology with lung function in 36 patients undergoing thoracotomy for a localized lesion. With increasing cumulative consumption, both inflammation and fibrosis of the respiratory bronchioles increased. Furthermore, airflow obstruction, as measured by the ratio of FEV₁ to FVC or by the maximum midexpiratory flow rate (FEF_{25-75%}), progressively decreased and residual volume increased with the amount smoked. Physiological measures of airflow obstruction correlated with the severity of small airways abnormalities.

The major parenchymal injury associated with cigarette smoking is emphysema: "abnormal dilation of air spaces distal to the terminal bronchioles accompanied by destruction of air space walls" (US DHHS 1984, p. 119). Emphysema and small airways injury contribute to the physiological impairment found in COLD; in individual patients with COLD, either may be predominant, but both are probably important in most (US DHHS 1984). By itself, emphysema is accompanied by spirometric evidence of airflow obstruction, increased lung compliance, and increased total lung capacity (TLC) and residual volume (RV). The diffusing capacity for carbon monoxide varies inversely with the extent of emphysema (Park et al. 1970; Cotes 1979). Emphysema is also associated with abnormalities of gas exchange.

Cigarette smoking, through its effects on the small airways and lung parenchyma, produces the clinical syndrome of expiratory flow limitation with dyspnea. The chronic airflow obstruction found in COLD develops progressively and insidiously in most cases through a sustained excessive decline of ventilatory function (US DHHS 1984). In COLD, spirometry shows reduced FEV₁ and a reduced FEV₁ to FVC ratio; FVC may also be diminished. The airflow obstruction is accompanied by increases in RV and TLC (Boushy et al. 1971; Cotes 1979).

Injury From Occupational Exposures

For occupational exposures in the absence of cigarette smoking, the patterns of lung injury vary among the agents, presumably on the basis of differences in their physical and chemical properties. Although the clinical and physiological manifestations of occupational lung injury may be distinct from those of cigarette smoking, overlap occurs for some exposures.

As with cigarette smoke, chronic irritation of the large airways by dusts and gases is associated with mucous gland enlargement and mucus hypersecretion (Morgan 1978, 1984b). This pattern of injury has been well documented clinically and pathologically for coal and cotton dust (Douglas et al. 1982; Edwards et al. 1975; Kibelstis et al. 1973; Merchant et al. 1972). Gold miners and grain workers also develop chronic bronchitis attributable to occupational dust exposure (Irwig and Rocks 1978; Dosman et al. 1980).

Industrial bronchitis may be associated with airflow obstruction. Hankinson and colleagues (1977) studied approximately 9,000 coal miners from 1973 to 1974. Among the nonsmoking miners with dust-induced bronchitis, decreased airflow at high lung volumes was demonstrated, a finding suggestive of changes in the larger airways.

Abnormalities of the small airways seem to be one of the earliest responses to mineral dust exposure (Churg et al. 1985). In a recent study of hard-rock miners and people employed in the asbestos, construction, and shipyard industries, Churg and colleagues (1985) showed that the abnormalities of the respiratory bronchioles associated with mineral dust are accompanied by airflow abnormalities. The lesions consisted of fibrosis and pigmentation in the small airways and were considered by these researchers to represent a nonspecific response to dust.

Involvement of the small airways has also been demonstrated in workers with specific exposures. For example, the coal macule is characterized by the deposition of alveolar macrophages loaded with coal dust in the respiratory bronchioles (Morgan 1984a). Subsequently, the involved respiratory bronchioles dilate, a change termed "focal emphysema" (Morgan 1984a). At this stage, individuals usually are asymptomatic and have no physical findings. The chest x